PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:
100031
Suite 602,Jinyu Tower A129 West Xuan Wu Men Street, XiCheng District, Beijing 100031,P.R.China
JEEKAI&PARTNERS
GUAN, Chang

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43 *bis*.1)

Date of mailing (*day/month/year*): 30 JUN 2005 (30.06.2005)

Applicant's or agent's file reference	FOR FURTHER ACTION
PCGNA50009	see paragraph 2 below

International application No.	International filing date (*day/month/year*)	Priority date (*day/month/year*)
PCT/CN2005/000387	28.Mar.2005(28.03.2005)	26.Mar.2004(26.03.2004)

International Patent Classification (IPC) or both national classification and IPC
G01N33/543

Applicant
CAPITALBIO CORPORATION et al.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No.II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i)with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No.VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No.VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/CN	Date of completion of this opinion	Authorized officer
The state Intellectual Property Office, the P.R.China 6 Xitucheng Rd., Jimen Bridge, Haidian District, Beijing, China 100088 Facsimile No. 86-10-62019451	31.May.2005(31.05.2005)	Shi Jianping Telephone No. 86-10-62085767

Form PCT/ISA/237(cover sheet)(April 2005)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/CN2005/000387

Box No. I Basis of the opinion

1. With regard to the language, this opinion has been established on the basis of:

   ☒ the international application in the language in which it was filed
   ☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material
      ☐ a sequence listing
      ☐ table(s) related to the sequence listing

   b. format of material
      ☐ on paper
      ☐ in electronic form

   c. time of filing/furnishing
      ☐ contained in the international application as filed.
      ☐ filed together with the international application in electronic form.
      ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ in addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No. PCT/CN2005/000387

Box No. V **Reasoned statement under Rule 43*bis*.1(a)(I) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement:

Novelty (N)	Claims	4,5,7,8,10,16,17,21-25	Yes
	Claims	1-3,6,9,11-15,18-20	No
Inventive step (IS)	Claims	4,23,24	Yes
	Claims	1-3,5-22,25	No
Industrial applicability (IA)	Claims	1-25	Yes
	Claims		No

2. Citations and explanations

Reference is made to the following documents, previously cited in the International Search Report.

D1=US, A, 2004038428;

D2=WO, A, 0225630;

D3=CN, A, 1435488.

(1) The subject-matter of independent claim 1 refers to a biochip for detecting a small molecule compound.

D1 discloses a microarray of smaller molecules, such as those less than 5,500 Da, which comprises a solid support and BSA carrier that is immobilized on a surface of the support. The carrier and smaller molecule form conjugate.

Thus it can be seen D1 discloses all features of claim 1, and D1 and claim 1 are in the same art, solve the same technological problems and have the same purpose. So claim 1 lacks novelty under PCT Article 33(2).

(2) The dependent claim 2,3,6,9 lack novelty under PCT Article 33(2) as the prior art as applied in the D1.

(3) The feature of the dependent claim 5,7,8 is that the small molecule compound is a prohibited substance such as amphetamine etc., and the biochip further comprises a control. D2 discloses a microfabricated ultrasound array through which durgs of abuse (i.e. prohibite substances) can be found. And the microfabricated ultrasound array comprises solid support and analyte bound on the surface of the support. More than one site in the microarray can be used as a control or reference to determine reference values for the assay. Thus, the dependent claim 5,7,8 lack an inventive step under PCT Article 33(3) as being obvious over the prior art as applied in the D1 and D2.

(4) The subject-matter of independent claim 10 refers to a method of making a biochip for detecting a small compound.

D1 discloses a microarray of smaller molecules and its manufacturing, which includes steps: attaching a molecular monolayer of BSA to the surface of the solid support; then spotting small molecule compound onto the modified surface of the support to form a conjugate of small molecule compound and BSA carrier.

And the method of claim 10 further includes drying the spotted solid support. D3 discloses fabrication of a biochip on which the small molecule compound can be immobilized. The last step of the method is drying the spotted biochip. It would be obvious to a skilled person in the art to apply D3 to the manutacturing method in D1. So claim 10 lacks an inventive step under PCT Article 33(3).

(5) The subject-matter of independent claim 11 refers to method for detecting a small molecule compound in a sample.

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of :V

As mentioned in opinion (1), D1 has disclosed the biochip in claim 1, and also a detection for small molecule compound with it. The detection comprises incubating the microarray with sample and binding molecule that specifically binds to the small molecule compound, such as antibody of the small molecule; detecting the binding of the binding molecule to the small molecule compound in the conjugate immobilized on the surface of the biochip, then the presence or absence or the quantity of the small molecule in the analyte.

Thus it can be seen D1 discloses all features of claim 11, and D1 and claim 11 are in the same art , solve the same technological problems and have the same purpose. So claim 11 lacks novelty under PCT Article 33(2).

(6) The dependent claim 12-15,18-20, lack novelty under PCT Article 33(2) as the prior art as applied in the D1.

(7) The feature of claim 16,21,22 are that the method further comprises the steps of comparing and incubating with a seccondary antibody. It is known by the skilled person in the art that comparing the binding of binding molecule to small molecule with the binding of the binding molecule to a control and using a secondary antibody linked to a label. Thus, the dependent claim 16,21,22 lack an inventive step under PCT Article 33(3) as being obvious over the prior art as applied in the D1 and the common knowledge.

(8) The feature of claim 17 is that the control is selected from the group of a blank control etc. D2 discloses that more than one site in the microarray can be used as a control or reference to determine reference values for the assay. Thus, the dependent claim 17 lacks an inventive step under PCT Article 33(3) as being obvious over the prior art as applied in the D1, D2 and the common knowledge.

(9) The subject-matter of independent claim 25 refers to a kit for detecting a small molecule compound in a sample.

D1 discloses a microarray of smaller molecules, such as those less than 5,500 Da, which comprises a solid support and BSA carrier that is immobilized on a surface of the support. The carrier and smaller molecule form cojugate. And a binding molecule can specifically bind to the small molecule compound to form binding complex.

And claim 25 restricts that the agents and equipment construct a kit. The skilled person in the art knows that agents and equipment used in assay can construct a kit and such a kit is familiar to the art person. It would be obvious to a skilled person in the art to apply the common knowledge to the biochip and agents in D1. So claim 25 lacks an inventive step under PCT Article 33(3).